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Short-term outcome of early electrical cardioversion for atrial fibrillation in hyperthyroid *versus* euthyroid patients*

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Abstract

Background: *Atrial fibrillation (AF) is the most common cardiac complication of hyperthyroidism. The influence of the time of cardioversion on hyperthyroidism-induced AF remains unclear. The aim of this study was to compare short-term outcomes of early electrical cardioversion for AF in hyperthyroid and euthyroid patients.*

Methods and Results: *Sixty-seven subjects with persistent AF (duration, 10 days–12 months) were divided into two groups according to thyroid function: Euthyroid (Group 1, n = 36, female/male: 23/13, mean age: 61.77 ± 10.45 years) and hyperthyroid (Group 2, n = 31, female/male: 10/21, mean age: 65.43 ± 6.40 years). Two patients were excluded for unsuccessful cardioversion (one in each group). In Group 2, 19 patients had clinical and 11 had subclinical hyperthyroidism. Following transthoracic and transesophageal echocardiography, cardioversion was performed until the highest energy was reached (270 J) or until sinus rhythm was achieved. AF recurrence was detected in 13 of 35 patients (37.1%) in Group 1 and in 11 of 30 patients (36.9%) in Group 2 (p = 0.96) at one month. Recurrence rate was higher in the clinical hyperthyroid patients than in the subclinical hyperthyroid patients (52.6% vs 9.1%, p = 0.021), but neither the clinical nor the subclinical hyperthyroid subgroups were significantly different from Group 1 in terms of recurrence rate (p = 0.27 and p = 0.13, respectively).*

Conclusions: *Electrical cardioversion should be performed for patients with persistent AF and hyperthyroidism as soon as possible.* (Cardiol J 2012; 19, 1: 53–60)

Key words: atrial fibrillation, cardioversion, hyperthyroidism

Introduction

Atrial fibrillation (AF) is the most common cardiac complication of hyperthyroidism [1, 2]. The prevalence of AF is 10% to 15% in hyperthyroid patients without heart disease, compared to 4% in the general population [3–5]. Prevalence increases to 25–40% for hyperthyroid patients aged over 60 years [5]. Besides clinical hyperthyroidism, subclinical hyperthyroidism is associated with a 3–5--fold increased risk of AF [5–8].

Atrial fibrillation in hyperthyroidism is associated with significant mortality and morbidity due to the high incidence of thromboembolic events and

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heart failure, especially in the elderly [3, 4, 9, 10]. The risk of arterial embolism in particular is higher during active thyrotoxicosis than on reversion to sinus rhythm (SR), and on euthyroid state [9]. It was recently shown that patients with hyperthyroidism-induced AF have a significantly greater risk of ischemic stroke (9.4%) than hyperthyroid patients without AF (0.6%) and AF patients without hyperthyroidism (3.1%), particularly within the first 30 days after AF diagnosis [11]. Furthermore, the risk of thromboembolic events increases with the duration of AF. Therefore, restoring SR as early as possible is crucial to decrease the risk of fatal complications in hyperthyroid patients with AF.

The general approach to the treatment of patients with hyperthyroidism-induced AF is to treat the hyperthyroidism, which results in conversion to SR in up to two-thirds of patients [4]. Patients restore SR within 8–10 weeks after achieving euthyroid state [4, 12], which is a long period considering the high risk of thromboembolic events. Cardioversion is generally suggested for patients remaining in AF after achieving euthyroid status [3, 4, 12–14].

The recurrence rate in the medium- (1–2 years) and long-term (over two years) following cardioversion for hyperthyroidism-induced AF has been reported to be lower, at around 40–60% [14––16], than the more than 80% recurrence rate in euthyroid patients [16]. Previous studies have reported the short-term (≤ one month) recurrence rate of AF after cardioversion to be 35–60% [17, 18]. But short-term recurrence of AF after cardioversion in hyperthyroid patients has not been studied so far. If hyperthyroidism-induced AF carries a similar short-term recurrence rate as AF of non-thyroid origin after conversion to SR, early electrical cardioversion should be considered for hyperthyroid patients.

In this study, we aimed to determine the short--term outcome of early electrical cardioversion for AF in hyperthyroid patients compared to euthyroid patients.

Methods

Study design and population

The study was designed as a prospective, controlled study. Sixty-seven subjects who were referred to the Cardiology Clinic of Bursa Yuksek Ihtisas Education and Research Hospital between January 2006 and August 2007 for persistent AF lasting longer than seven days were included in the study. The exclusion criteria were: New York Heart Association (NYHA) class III–IV congestive heart failure [19], significant native or prosthetic valvular disease, previous valve surgery, previous electrical or medical cardioversion for AF, significant left ventricular dysfunction, severe left atrial enlargement (> 5 cm) and left atrial thrombus in transesophageal echocardiography (TEE), paroxysmal AF, sick sinus syndrome, or any contraindication for anticoagulation. However, during the initial evaluation period, patients with hyperthyroidism and disorders of thyroid function test which were related to chronic disease, and patients taking antithyroid drugs and amiodarone were excluded. One hundred and thirty three patients had been assessed for their suitability for the study over the 19 months. Sixty six of the 133 (49.6%) patients were excluded from the study: 26 because they had significant valvular heart disease, 22 patients had NYHA class III–IV congestive heart failure, three patients had left atrial thrombus, five patients had previous electrical or medical cardioversion, and ten patients were taking amiodarone. Fifteen of the 66 patients (22.7%) had hyperthyroidism and the other 51 (77.3%) had normal thyroid function test. After excluding these 66, 67 patients (50.4%) were accepted into the study, and these were divided into two groups according to the thyroid function test. Of the study population of 67, 36 patients with normal thyroid function test formed Group 1, and the other 31 patients, with hyperthyroidism, formed Group 2. Two patients were excluded due to unsuccessful cardioversion (one from each group), meaning that a total of 65 patients (97% of the 67 patients who were successfully converted; 35 patients in Group 1 and 30 patients in Group 2) were studied.

Patients gave informed consent prior to any study-related procedures. The study was approved by the local ethics committee of Bursa Yuksek Ihtisas Education and Research Hospital, and conducted in accordance with the latest version of the Helsinki Declaration and local regulations.

Study procedures

Initial evaluation of patients included detailed medical history, physical examination, and thyroid function tests, which are free triiodothyronine (T3), free thyroxine (T4), and thyroid stimulating hormone (TSH, thyrotropin) levels. Patients with low TSH levels were deemed to have hyperthyroidism. These patients formed Group 2 and they were further divided into clinically evident hyperthyroidism (low TSH levels and high free T3 and T4 levels) or subclinical hyperthyroidism (low TSH levels and normal free T3 and T4 levels) sub-

groups (normal range of: TSH levels: 0.34–5.60 μIU/mL, free T3 levels: 2.50–4.20 pg/mL, free T4 levels: 0.58–1.64 pg/dL).

Echocardiographic evaluation

For all patients, transthoracic echocardiography (TTE) and TEE were performed before cardioversion as suggested by the American Society of Echocardiography. TTE was also performed at one hour, 24 hours and one month for conventional echocardiographic measurements after restoring SR with cardioversion. During echocardiographic evaluation, 3.5 Mhz probe was used at Vivid 7 Pro TTE (GE Vingmed, Horten, Norway) and multiplane 6 Mhz probe was used at TEE. Left atrium and left ventricle were measured at parasternal long-axis view. Left ventricular ejection fraction was calculated by echocardiography using the modified Simpson's method. Left atrial appendage was clearly viewed with TEE in all patients. The presence of thrombus or spontaneous echo contrast at left atrial appendage was evaluated by two-dimensional TEE. For the assessment of contractile functions, pulse wave Doppler was placed in the proximal one third of the left atrial appendage. In patients with AF, left atrial appendage filling and emptying velocities were obtained by the arithmetic mean of eight consecutive measurements. None of the patients had any complication during TEE.

Maximum flow rates at aortic, mitral, and tricuspid valves were measured using apical four-chamber and five-chamber views in pulsed Doppler assessment. Atrial function after cardioversion was evaluated conventionally by calculating the peak velocity of the early diastolic wave (E) and peak velocity of the late diastolic wave (A), their ratio (peak E/A), and the time-velocity integrals of the peak velocities of the early and late diastolic waves with pulsed Doppler that was recorded from the apical four-chamber view, with the sample volume positioned between the tips of the mitral and tricuspid leaflets in parallel to ventricular inflow.

Cardioversion procedure

Acetylsalicylic acid and intravenous unfractionated heparin (17 U/kg, Nevparin 25,000 IU, MN Pharmaceuticals, Istanbul, Turkey) were given to all patients before cardioversion to obtain target partial thromboplastin time of 1.5–2 times normal. Patients in Group 1 who did not have intracardiac thrombus in TTE and TEE evaluation were given intravenous amiodarone (loading dose, 5 mg/kg; maintenance dose, 10–15 mg/kg/h for 24 h). Patients in Group 2 were given beta-blocker as esmolol infusion (loading dose, 500 mg/kg for 1 min; maintenance dose, 0.05 mg/kg/min with 0.05 mg/kg/min increments every 5 min according to ventricular rate to reach a maximum dose of 0.2 mg/kg/min) followed by 50–100 mg oral metoprolol and propylthiouracil (loading dose, 150–300 mg/day for clinical hyperthyroidism or 100 mg/day for subclinical hyperthyroidism; maintenance dose was determined according to clinical response). Antiarrhythmic agents and digoxin were stopped before cardioversion, but antithyroid therapy continued for patients in Group 2. Sedation was obtained with intravenous midazolam (following the initial dose of 3 mg, 1-mg injections until sedation) before cardioversion. Transthoracic electrical direct current (DC) cardioversion was applied to patients under intensive care unit conditions by giving synchronized biphasic DC with cardioverter-defibrillator (Cardiolife TEC 5531 Nihon Kohden Corporation, Japan). The level of energy for cardioversion was 150 J initially, and 200 J and 270 J subsequently. External biphasic DC shocks were used at the physician's discretion until the highest energy was reached (270 J) or until SR was restored. The cardioversion was defined as successful if SR lasted longer than one minute following cardioversion. Patients restoring SR had effective anticoagulation (international normalized ratio [INR] higher than 2.0) with warfarin (following the initial dose of 5 mg/day, dose was adjusted to obtain INR as 2–3) after cardioversion for one month. Heart rate and rhythm were monitored using an electrocardiography (ECG) monitor and 12-lead ECG.

Amiodarone was continued after discharge from hospital (orally 200 mg/day for four weeks). Patients were evaluated at one, two, and four weeks after discharge by physical examination, ECG, and INR.

Statistical analysis

SPSS software for Windows (Version 11.5, 2003, SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Data was presented as mean ± ± standard deviation (SD). Categorical variables were compared using the Pearson χ^2 test and Fisher's exact test; continuous variables were compared using Student t test (for normally distributed data) or Mann-Whitney U test (for other data). The correlation between the maintenance of SR and other parameters were evaluated with a Pearson's correlation analysis. Statistical significance level was defined as $p < 0.05$.

Table 1. Basic demographic and clinical characteristics of patients in Group 1 and Group 2.

	Group 1 (control, n = 35)	Group 2 (hyperthyroidism, n = 30)	P
Age [years]	61.77 ± 10.45	65.43 ± 6.40	0.10
Gender (men/women)	13 (37.1%)/22 (62.9%)	21 (70%)/9 (30%)	0.008
Duration of atrial fibrillation [days]	192.94 ± 146.64	182.16 ± 125.84	0.75
Initial heart rate [bpm]	109.02 ± 20.54	112.13 ± 18.43	0.52
Body surface area [m^2]	1.79 ± 0.19	1.73 ± 0.16	0.17
Systolic blood pressure [mm Hg]	138.14 ± 17.66	140.63 ± 17.13	0.56
Diastolic blood pressure [mm Hg]	85.14 ± 10.60	86.83 ± 9.51	0.50
Chronic diseases:			
Diabetes mellitus	3 (8.6%)	0 (0%)	0.10
Hypertension	28 (80%)	23 (76.7%)	0.74
Dislipidemia	3 (8.6%)	2 (6.7%)	0.77
Coronary artery disease	1 (2.9%)	0 (0%)	0.35
Smoking	3 (8.6%)	5 (16.7%)	0.32
Drugs:			
Acetylsalicylic acid	32 (91.4%)	28 (93.3%)	0.77
Beta-blocker	23 (65.7%)	26 (86.7%)	0.051
Calcium channel blocker	1 (2.9%)	1 (3.3%)	0.91
ACE inhibitor	27 (77.1%)	23 (76.7%)	0.96
Angiotensin receptor blocker	3 (8.6%)	1 (3.3%)	0.38
Antilipidemic	1 (2.9%)	0 (0%)	0.35
Diuretic	1 (2.9%)	0 (0%)	0.35

Data is given as mean ± standard deviation or n (%)

Results

Demographic and clinical findings

There was no difference in the mean age of patients between Group 1 and Group 2 (61.77 ± ± 10.45 years *vs* 65.43 ± 6.40 years, respectively, p = 0.10), but the percentage of men in Group 2 was significantly higher than Group 1 (70% *vs* 37.1%, p = 0.008; Table 1). Duration of AF was between ten days and 12 months for both groups (192.94 ± 146.64 days for Group 1 and 182.16 ± ± 125.84 for Group 2, p = 0.75). Study groups were comparable in terms of other baseline clinical findings, which were initial heart rate, body surface area, blood pressure, concomitant chronic diseases, and drugs used (Table 1).

According to laboratory evaluation of thyroid function, mean TSH level was 2.46 ± 1.42 and 0.028 ± 0.024 (p < 0.001), free T3 level was 2.57 ± ± 0.56 and 6.22 ± 5.29 (p = 0.001), and free T4 level was 1.16 ± 0.13 and 2.25 ± 1.18 (p < 0.001) for euthyroid patients in Group 1 and patients in Group 2. Clinically evident hypert hyroidism was determined in 19 patients and subclinical hyperthyroidism was determined in 11 patients in Group 2. Elevated antithyroperoxidase antibody titers and antithyroglobulin antibody titers were detected in ten (33%) patients and six (20%) patients, respectively. Graves's disease was the underlying cause of hyperthyroidism in two (6.7%) patients, and multinodular goiter accounted for the remaining 28 (93.3%) patients. At one month clinical follow-up, we did not see transient ischemic attack, stroke, or death in either group.

Echocardiographic findings

Left ventricular ejection fraction was 63.34 ± ± 5.81% for Group 1 and 60.66 ± 5.88% for Group 2 (p = 0.41). Left atrium diameter was 4.38 ± 0.32 cm and 4.41 ± 0.37 cm for Group 1 and Group 2, respectively (p = 0.75). Other echocardiographic parameters before cardioversion were also similar in Group 1 and Group 2 (Table 2).

There was no significant difference between Group 1 and Group 2 in terms of left atrial appendage outflow or inflow velocities (Table 2). Mitral E velocity (0.79 ± 0.16 ms for Group 1 and 0.79 ± 0.14 ms for Group 2, p = 0.99) and tricuspid E velocity (0.48 ± 0.28 ms for Group 1 and 0.50 ± ± 0.12 ms for Group 2, p = 0.36) in pulsed Dop-

Table 2. Echocardiographic findings in Group 1 and Group 2.

	Group 1 (control, n = 35)	Group 2 (hyperthyroidism, n = 30)	P
Left atrium diameter [cm]	4.38 ± 0.32	4.41 ± 0.37	0.75
Left ventricular end-systolic diameter [cm]	3.19 ± 0.12	3.28 ± 0.16	0.37
Left ventricular end-diastolic diameter [cm]	4.80 ± 0.65	4.72 ± 0.11	0.54
Septal wall thickness [cm]	1.13 ± 0.14	1.18 ± 0.17	0.24
Posterior wall thickness [cm]	1.11 ± 0.12	1.13 ± 0.12	0.48
Left ventricular ejection fraction [%]	63.34 ± 5.81	60.66 ± 5.88	0.41
Fractional shortening [%]	33.65 ± 4.77	32.03 ± 5.50	0.20
End-systolic volume [mL]	32.71 ± 10.16	37.26 ± 13.90	0.13
End-diastolic volume [mL]	93.97 ± 20.78	99.03 ± 24.72	0.37
Pulmonary artery pressure [mm Hg]	40.62 ± 8.23	43.36 ± 10.42	0.26
LA appendage peak outflow velocity [cm/s]	0.48 ± 0.12	0.49 ± 0.07	0.73
LA appendage mean outflow velocity [cm/s]	0.38 ± 0.10	0.38 ± 0.06	0.97
LA appendage peak inflow velocity [cm/s]	0.50 ± 0.13	0.51 ± 0.08	0.82
LA appendage mean inflow velocity [cm/s]	0.40 ± 0.09	0.41 ± 0.07	0.90
Mitral E velocity [m/s]	0.79 ± 0.16	0.79 ± 0.14	0.99
Tricuspid E velocity [m/s]	0.48 ± 0.28	0.50 ± 0.12	0.36
Mitral A velocity at one hour [m/s]	0.43 ± 0.16	0.47 ± 0.16	0.42
Tricuspid A velocity at one hour [m/s]	0.35 ± 0.18	0.34 ± 0.17	0.86
Mitral E/A ratio at one hour	2.02 ± 0.79	1.83 ± 0.63	0.31
Tricuspid E/A ratio at one hour	1.44 ± 0.44	1.49 ± 0.40	0.63
Mitral A time-velocity integral at one hour [cm]	4.65 ± 2.00	4.79 ± 1.73	0.77
Mitral A velocity at 24 hours [m/s]	0.50 ± 0.17	0.67 ± 0.26	0.24
Left atrium diameter at one month [cm]	4.21 ± 0.30	4.29 ± 0.32	0.45

Data is given as mean ± standard deviation; LA — left atrial; E — early diastolic wave; A — late diastolic wave

pler were comparable between the study groups. Atrial function parameters at one hour (mitral A velocity, tricuspid A velocity, mitral E/A ratio, tricuspid E/A ratio, and mitral A time-velocity integral), at 24 h (mitral A velocity), and at one month (left atrium diameter) after cardioversion were also similar between Group 1 and Group 2 (Table 2).

Cardioversion and recurrence of atrial fibrillation

For all patients, SR was restored immediately after cardioversion and was maintained for 30 min.

The mean total energy of cardioversion was 221.42 ± 46.15 J in Group 1 and 215.66 ± 46.06 J in Group 2 ($p = 0.61$). Patients were followed up to one month. Atrial fibrillation recurrence rate was similar in Group 1 and Group 2 at the end of the first month; recurrence was detected in 13 of 35 patients (37.1%) in Group 1 and in 11 of 30 patients (36.9%) in Group 2 ($p = 0.96$) at the end of the first month (Fig. 1). No complication was recorded in patients who received anticoagulant treatment for one month following cardioversion.

The AF recurrence rate at the end of the first month was significantly higher among patients with clinically evident hyperthyroidism than patients with subclinical hyperthyroidism in Group 2 (52.6% and 9.1%, respectively, $p = 0.023$). However, there was no statistically significant difference in AF recurrence rates between patients with clinically evident hyperthyroidism and Group 1 (52.6% and 37.1%, respectively, $p = 0.27$) and patients with subclinical hyperthyroidism and Group 1 (9.1% and 37.1%, respectively, $p = 0.13$; Fig. 1).

According to correlation analysis, we found a significant negative correlation between SR maintenance and duration of AF ($r = –0.48$, $p < 0.001$) and corrected left atrial diameter according to body surface area ($r = –0.27$, $p = 0.02$) but we did not show a significant correlation between SR maintenance and age ($r = –0.10$, $p = 0.42$), TSH ($r = –0.10$, $p = 0.41$), free T3 ($r = –0.07$, $p = 0.56$), or free T4 ($r = –0.16$, $p = 0.18$) levels.

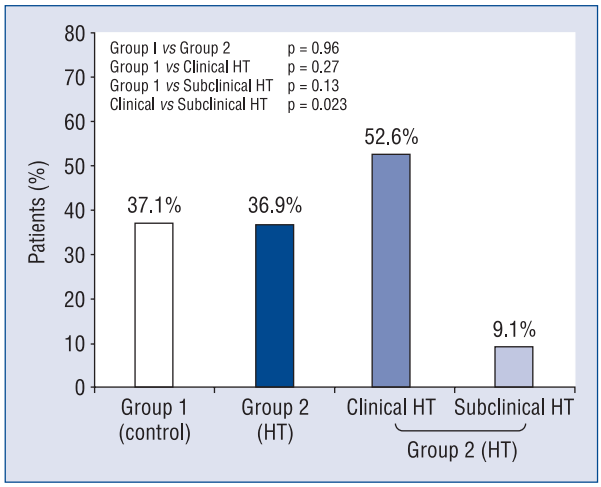

Figure 1. Atrial fibrillation recurrence rate at the end of the first month among patients in Group 1 (control, n = 35), Group 2 (hyperthyroidism, n = 30), and subgroups of Group 2, which were clinically evident hyperthyroidism (n = 19) and subclinical hyperthyroidism (n = 11); HT — hyperthyroidism.

Discussion

In this prospective, randomized, parallel group, and controlled study, we evaluated the short-term (one month) outcome of early electrical cardioversion in hyperthyroidism-induced AF compared to euthyroid AF. We found that the short-term outcome of early electrical cardioversion is similar in hyperthyroid and euthyroid patients, suggesting that early electrical cardioversion may be applied for hyperthyroidism-induced AF even before euthyroid status is achieved.

Cardiac events associated with hyperthyroidism, the most common of which is AF, are the most frequent and most serious complications of the disease. In a population-based study on 40,628 patients with hyperthyroidism, 8.3% had AF or flutter within 30 days of the diagnosis of hyperthyroidism [20]. Hyperthyroid patients with male sex, increasing age, ischemic heart disease, congestive heart failure, and heart valve disease have a particularly increased risk of AF [20]. In another large study including more than 23,000 subjects, AF was detected in 2.3% of euthyroid subjects, and in 12.7% and 13.8% of the subjects with subclinical and overt hyperthyroidism, respectively [6].

Patients with hyperthyroidism and without heart disease have an increased incidence of abnormal supraventricular premature depolarizations and nonsustained tachycardias [21]. The main mechanisms for the increased risk of AF in hyperthyroidism are alterations in cellular membrane function causing shortening of the atrial refractory period, triggered activity in the pulmonary vein cardiomyocytes, increased supraventricular ectopic activity, and activation of these arrhythmogenic foci by elevated thyroid hormones [4, 5, 21]. Thyroid hormones act directly through nuclear thyroid receptors causing increased gene transcription of cardiac myocyte proteins [4]. Thyroid hormones increase heart rate, ventricular contractility and cardiac hypertrophy by upregulating sarcoplasmic calcium ATPase which plays a central role in myocardial contractility [22], myosin heavy chain alpha, voltage gated K+ channels, Na+ channels and beta1 adrenergic receptors [4]. However, as we have previously reported [23], left atrial appendage functions evaluated by TEE are not altered in patients with hyperthyroidism.

Atrial fibrillation is an independent risk factor for cardiovascular thromboembolic events [9]. It carries a 3–6% risk of thromboembolic complications, which is 5–7 times greater than that of subjects with SR [24]. Atrial fibrillation increases the risk of blood clot formation inside the heart due to rapid and irregular heartbeat causing embolism, stroke, silent cerebral infarction and other disorders [9]. Siu et al. [11] recently showed that there was an increased risk of ischemic stroke for hyperthyroid patients with new-onset AF during the early phase following diagnosis. Therefore, hyperthyroidism-induced AF should be treated promptly. The general treatment approach is antithyroid therapy and elective cardioversion for patients who maintain a euthyroid state but are still in AF [3, 12]. Atrial fibrillation usually disappears upon normalization of T4 and T3 hormone levels with antithyroid treatment [12]. Systemic anticoagulation is also indicated in the presence of AF to prevent fatal complications, and should be continued until SR has been present for at least three months [2, 25]. Although most patients respond to this treatment approach, patients are at high risk of thromboembolic complications and may need to be treated with anticoagulants for long periods until SR is restored. Therefore, many authors have suggested early cardioversion in the treatment of hyperthyroidism--induced AF, taking into account the medium- and long-term outcomes of patients [16].

Since duration of AF is the main determinant of duration and severity of atrial stunning [26], restoring SR as early as possible reverses atrial stunning and thus decreases the risk of thromboembolic complications. Therefore, early electrical cardioversion before antithyroid therapy should be

considered for hyperthyroidism-induced AF to minimize the risk of thromboembolic complications.

Nakazawa et al. [15] evaluated the outcome of cardioversion in patients with thyrotoxicosis-induced AF for a median duration of 28.5 months. They reported that 98 out of 106 patients were successfully cardioverted and at late follow-up (mean 80.6 months), 67% were in SR [15]. In a recent study by Siu et al. [16], the AF recurrence rate during a 24 month follow-up period after successful electrical cardioversion was 59% for patients with hyperthyroidism-induced AF, *vs* 83% in AF of non-thyroid origins ($p = 0.04$).

Thus, hyperthyroidism-induced AF carries a lower recurrence rate after conversion to SR than non-hyperthyroidism-induced AF, and early electrical cardioversion should be considered. But the outcome of early electrical cardioversion performed without waiting for a euthyroid state has not been reported in the literature. In the present study, we aimed to determine the short-term outcome of early electrical cardioversion in hyperthyroidism-induced AF.

We found that AF recurrence rate was similar in euthyroid and hyperthyroid groups at the end of the first month (37.1% *vs* 36.9%, respectively, $p = 0.96$). In other words, 62.9% of euthyroid patients and 63.3% of hyperthyroid patients were at SR at one month following cardioversion. The short-term (≤ one month) recurrence rate of AF after cardioversion in our study was similar to the rates reported in the literature. Ari et al. [27] showed that 20 of 58 patients (34.5%) with persistent AF reverted to AF during the six months following successful electrical cardioversion. Vikman et al. [17] reported a one month recurrence rate of 35% among 78 patients with persistent AF after restoration of SR with electrical cardioversion. Tieleman et al. [18] reported a higher recurrence rate during one month of follow-up: 35 out of 61 patients (57%) had a relapse of AF in their study. The variability in the short-term recurrence rate following cardioversion in these studies may be explained with differing baseline patient characteristics such as advanced age [28] and duration of AF study populations [17, 18].

It should also be noted that Group 1 was treated with amiodarone, while Group 2 was given beta-blocker due to the negative effects of amiodarone on thyroid functions. It is remarkable that although amiodarone is effective [29], and superior to beta-blockers in preventing AF recurrence [30], euthyroid and hyperthyroid groups showed similar recurrence rates in our study.

Another important finding of our study is that the AF recurrence rate at one month was significantly higher in clinically evident hyperthyroidism than subclinical hyperthyroidism (52.6% and 9.1%, respectively, $p = 0.023$). However, neither the clinically evident hyperthyroidism group nor the subclinical hyperthyroidism group was not shown statistically significant difference from the euthyroid control group in terms of AF recurrence rate ($p = 0.27$ and $p = 0.13$, respectively). This shows that early electrical cardioversion may be applied in patients with both clinical and subclinical hyperthyroidism, but it may be more effective in patients with subclinical hyperthyrodism for prevention of AF recurrence.

As shown in previous studies [17, 18], we found a significant correlation between SR maintenance and duration of AF and left atrial diameter. But we did not find a correlation between SR maintenance and thyroid function test. These results support the opinion that cardioversion should be performed in patients with persistent AF and hyperthyroidism as soon as possible.

The major limitations of this study were the small sample size and short follow-up duration. In spite of the limited number of patients, our study presents a treatment alternative for hyperthyroid patients with AF to prevent fatal complications. The preliminary findings of the present study should be confirmed by further controlled clinical studies with a larger sample size and longer follow-up duration to evaluate the medium- and long-term outcomes of early cardioversion in AF induced by hyperthyroidism.

Conclusions

The short-term (one month) recurrence rates following early electrical cardioversion for AF are similar for hyperthyroid and euthyroid patients. Thus, early electrical cardioversion should be considered for hyperthyroidism-induced AF, particularly for subclinical hyperthyroid patients, without waiting for a euthyroid state. This would decrease the risk of thromboembolic complications by restoring SR promptly. Further prospective studies with a large sample size are needed to confirm the advantages of early electrical cardioversion during treatment algorithm of hyperthyroidism-induced AF.

Conflict of interest: none declared

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